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## RELAPSE ASSOCIATED WITH DRUG RESISTANCE IN LEPROSY

When we think of drug resistance in leprosy we have to remember that resistance is one of the factors that may be listed as causes of relapse in people affected by leprosy. Statistical data has shown that in recent years the rates of relapse in leprosy in Brazil have remained around 4%<sup>4</sup>. Considering all forms of entry of cases into the national information system (SINAN), this rate has not been considered too high, which shows the effectiveness of the multidrug therapy (MDT) scheme.

Our experience in evaluating patients with suspected relapse associated with resistance to one or more drugs from the MDT scheme using Shepard's technique, shows that only a small percentage of cases are investigated annually. Among more than 1000 cases reported as relapses in the country, about 30 samples are annually evaluated at Lauro de Souza Lima (ILSL) e, which we consider a very small number to reflect the real situation of resistance in the country<sup>1</sup>. Moreover, many of the cases that come to us with suspected resistance are accompanied by inconsistent data, which leads us to question whether they are really cases of recurrence, according to the criteria established by the Ministry of Health.

The about 4% of cases include those which in the end of the treatment still had active lesions and /or solid bacilli; cases which we define as persisters (remain with persistent bacilli) which should have been subjected to repetition of the treatment regimen (12 additional doses of MDT / MB). Also, multibacillary cases misclassified as paucibacillary, which should have been treated with a MDT / MB.

Given the chronicity of the disease, the evaluation of recurrence is complex. How to assess drug resistance?

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How to study cases of bacillary persistence? How to address cases which completed the treatment regimen, but irregularly? Is it possible that relapse cases are in fact cases that became infected again by a different strain? What do we know about primary resistance?

When MDT was introduced in Brazil, there were a limited number of tools to evaluate transmission and therapeutic efficacy. Besides the techniques conventionally used as diagnostic support, such as the skin smear and histopathology, nowadays we can take advantage of techniques that give us more sensitive and rapid results, although more expensive, as the realtime PCR to quantify bacilli present in lesions, bacterial DNA sequencing to verify the presence of mutations associated with drug resistance, and study the genotypes of the bacteria present in lesions and thus relate them to patterns of transmission<sup>2,3</sup>.

The reports of resistance in leprosy in Brazil do not differ much from other countries when considering the percentage of resistance cases identified among reported relapses. Therefore, the rates show that resistance is not major problem in Brazil today. However,

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the number of new leprosy cases diagnosed has decreased slowly and is there are some areas still considered to be hyperendemic in the country. The presence of resistant strains being transmitted in these areas could hamper the control of the disease.

We know that there are geographically disadvantaged areas for referral of patients, and even manipulation of biological samples. However, it is necessary to develop strategies to better assess the causes of relapse in the country and readily identify cases of resistance. This way we will avoid it to become a problem of major importance for the country.

## REFERÊNCIAS

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